ACUTE PANCREATIC NECROSIS AND ITS SEQUELÆ

A CRITICAL STUDY OF THIRTY CASES

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The development of pancreatic surgery since Körte's treatise,[1] in 1898, through the monographs of Heiberg,[2] in 1914, Gross and Guleke,[3] in 1924, Schmieden and Sebening,[4] in 1928, up to its present status, described in Wolfer's[5] and Heller's[6] reviews, contains all the clinical bibliography on the subject. In spite of the vast amount of experimental work and case reports the uncertainty of diagnosis and the high mortality have remained practically unchanged. Table I includes only three large statistics, and shows that, in comparison with other fields in surgery, very little progress has been made in reducing the mortality of acute necrosis of the pancreas.

Table I

Mortality of Acute Pancreatic Necrosis

Author	Year	Number of Cases	Mortality Per Cent.
Körte	1911	103	60
Guleke	1924	437	52.2
Schmieden and Sebening	1927	1278	51.2

In the present study, thirty cases of acute pancreatic necrosis or their sequelæ were analyzed, that entered the Evanston and Wesley Memorial Hospitals between 1920 and 1930. It represents the material of nine surgeons and is thus a fair average of what a patient may expect when struck with acute necrosis of the pancreas and taken to a large general hospital. Obviously the pre-operative management, the diagnosis, the operation and after treatment were not uniform in this series; however, while on a small material, this offered an excellent basis of comparing various methods of management. As a close correlation of physiological and pathological data with clinical observations is singularly lacking in most of the publications, we tried to point these out, with the hope that they may aid in lowering the mortality and untoward sequelæ of this disease.

Age and Sex of Patients.—(Table II.) Half of the patients (fifteen) were between the ages of forty and sixty. Schmieden and Sebening mention the case of a thirteen-year-old girl with a common-duct stone, who developed an acute necrosis. Cases are on record at the ages of two and one-half, three, four and seven years.[7] However, the occurrence of the disease below twenty years must be very rare and was not observed in our series.

TABLE II

Age and Sex of Patients

Decades	Number of Cases
20–30	6
30–40	5
40–50	7
50–60	8
60–70	3
80–90	1
	30

Half of the patients were between the ages of 40–60.

Number of men	12
Number of women	18

The incidence of sex was twelve male to eighteen female patients. The slight preponderance of the female sex is present in all of the large statistics and is undoubtedly due to the important rôle of gall-bladder disease in the etiology.

The Clinical Picture.—Recurrent attacks of upper abdominal or right hypochondriac pains were elicited in nineteen patients, whereas eleven denied having any previous attacks. The clinical symptoms of the last attack for which the patient came to the hospital were as follows. (Table III.)

TABLE III

Clinical Signs and Symptoms of Acute Pancreatic Necrosis

Symptoms and Signs	Number of Cases
Pain in epigastrium with general irradiation	30
Reverse peristalsis (nausea, vomiting, acute gastric dilatation)	23
Jaundice or clay-colored stools	12
Pain in right upper quadrant and right shoulder	10
Pain in epigastrium, irradiating to the left	7
Muscle rigidity	3
Palpable mass	1

The pain of acute pancreas necrosis is excruciating. One of our own patients, who had just gone through childbirth, stated that this annihilating pain was far worse than anything she had ever experienced. While the radiation to the right upper quadrant and shoulder seem natural in view of the frequent association with gall-stones and common-duct stones, the irradiation to the left, mentioned in seven instances, requires some discussion. Katsch[8] emphasized that irradiation to the left in a gall-bladder colic is suggestive of pancreatic involvement. When one realizes that most of the gland lies to the left of the mid-line, an involvement of the body or tail of the pancreas may easily give such irradiation. It is probable that on careful questioning such a symptom and the occurrence of Head-zones on left-sided segments could be more often elicited.

Jaundice in twelve cases shows that obstruction of bile flow may frequently complicate the picture. Common-duct stone, cholangitis or a swelling of the head of the pancreas are the most commonly quoted causes. However, one must consider the possibility of a toxic hepatitis, a fatty degeneration of the liver or even an acute liver atrophy, as observed in one case of the present series. The serious general intoxication that follows autolysis of the pancreas may be responsible for the hepatic damage. Wolfer[9] has recently summarized and advanced new evidence of a possibility of pancreatic digestion of the biliary tract and liver substance through a backflow of pancreatic enzymes into the common duct in the etiology of certain types of cholecystitis. Whether such a mechanism could also operate during an attack of acute necrosis of the pancreas has not yet been investigated.[10] At present, the hepatic injury can be best explained by the severe intoxication with protein-split products or an ascending pylephlebitis. Uræmia in connection with hepatic damage has been reported,[11,12] and is part of the general intoxication in severe jaundice.

Muscle rigidity does not belong to the typical picture of acute necrosis of the pancreas. In all three cases of our series a diffuse, purulent peritonitis was present. Thus it must be considered as a late sign of serious prognostic value.

A palpable mass in the epigastrium was noted in one case. In thin individuals, with a gastroptosis, the normal pancreas can be palpated at times; swelling, or induration in such a patient, can be palpated a few hours after the onset. Usually, however, the gastric and colonic distention, which is an almost constant symptom of retroperitoneal exudates or hæmorrhages, prevents the palpation of any mass.

Laboratory Examinations.—Blood counts.—(Table IV.) Red blood counts above 5,000,000 were obtained in nine cases. The hemoglobin was correspondingly high. The counts were all taken on entrance to the hospital. The first seven cases were obviously dehydrated, had not taken enough fluids while being sick at home. These high counts would indicate the necessity of parenteral administration of fluids on entrance to the hospital. The last two cases with unusually high red counts must have been both in shock. Case XXIV entered the hospital in the middle of the night with a red count of 7,000,000. Next morning the count was 5,900,000. She was operated on the third day of her entrance and recovered. Case XXX entered the hospital with a count of 8,300,000 and a hemoglobin of 140 per cent., in "agony." The patient was operated on twelve hours after the onset of the attack and died forty-eight hours later. Twenty-four hours after the operation the red count was 5,650,000, with 94 per cent. hemoglobin. The value of interpreting these high red counts as an index of shock has not been utilized in pancreatic surgery. The difference between capillary and venous red cell counts should be a good estimate of the amount of shock,[13] and should certainly warn against immediate operation.

TABLE IV

Red Cell Counts Over 5,000,000 in Acute Pancreatic Necrosis

Case No.	Red cell count	Hemoglobin	Remarks
1	5,500,000	80	Vomited for three days
3	5,700,000	100	Nauseated—nothing by mouth for three days
4	5,208,000	100	No food or liquids for five days
14	5,400,000	70	Sick at home for nineteen days
16	5,650,000	98	Vomited for four days
20	5,440,000	95	Pyloric stenosis
21	5,400,000	90	Vomiting three days
24	7,000,000	?	Five hours after onset
30	8,300,000	140	In shock, ten hours after onset

An unusually low red count (2,230,000, with 55 per cent. hemoglobin) was obtained in Case VII, a deeply jaundiced patient, who died forty hours after the operation. Post-mortem revealed an acute yellow atrophy of the liver.

The other patients showed a moderate secondary anæmia, which is well explained by an elevated temperature, the chronic toxæmia and the fact that they had overcome the initial dehydration.

White Counts.—(Table V.) Leucocyte counts are available in every case and show a great deal of variation. The value of white counts in acute abdominal conditions is probably over-emphasized. So many factors, such as infection, hæmorrhage, shock, dehydration, influence it, so that it can be used only as supportive or additional evidence in diagnosis. Even acute pain produces a leucocytosis.[14] Nevertheless, in this small series it is obvious that white counts below 15,000 were observed either in patients with diffuse peritonitis, whose counts were 3,800 and 4,700 respectively, or in patients with late sequelæ of acute necrosis, such as cysts or chronic pancreatitis. It seems that all cases in the acute stage had a white count above 15,000 and that there were four cases with a count of over 30,000. Two of these patients had a fulminating gangrene and died, while two had late pancreatic abscesses and recovered.

TABLE V

Leucocyte Counts in Acute Pancreatic Necrosis and Its Sequelæ

White Count	Number of Cases	Remarks		
Below 5,000	4	Diffuse peritonitis	2	
		Chronic pancreatitis	2	
5,000–10,000	5	Chronic pancreatitis	3	
		Pancreatic cyst	2	
10,000–15,000	2	Chronic pancreatitis	2	
15,000–20,000	8	Subacute cases	6	
		Terminal in shock	2	
20,000–30,000	4	Acute biliary infection	2	
		Acute pancreatic necrosis	2	
Above 30,000	4	Hyperacute necrosis	2	(both died)
		Abscess of the pancreas	2	

Differential white counts were made in eight patients, three of which showed a neutrophil polymorphonuclear count of over 85 per cent. The differential white count, including the Schilling-Arneth count, has been studied by some authors.[15, 16] The shifting of the leucocytes to the immature forms seems a constant finding but is not specific and is found in any acute destructive process. Its prognostic value has been repeatedly emphasized by Schilling[17]; but only a few of our clinical technicians are trained to use it and its use has not become general.

Examination of the Urine.—Abnormal findings are listed in Table VI. The severe intoxication is again manifested by the frequent appearance of albumen and casts. The occurrence of glycosuria in four cases indicated a disturbance of the internal pancreatic secretion, although it is known that diffuse peritonitis may also produce it. Aceton and diacetic acid were found twice but probably were not determined in every case.

TABLE VI

Urinary Findings in Acute Pancreatic Necrosis

Missing reports	4
Negative	2
Albumen	11
Granular and hyalin casts	9
Sugar	4
Aceton plus diacetic acid	2
Red cells	2

Blood Sugar.—Such determinations are available in six cases, and gave the following readings (Table VII): Of the six cases, three were not acute; the other three were taken shortly after the operation and showed an elevation of blood sugar. In not one case was a pre-operative determination made.

TABLE VII

Blood-sugar Determinations in Acute Pancreatic Necrosis and Its Sequelæ

Case No.	Blood Sugar in mgs. per 100cc.	Remarks
2	75	On sixth post-operative day, two days before death
17	95	Chronic pancreatitis; two years after cholecystectomy
20	92.7	Sclerosis of the head of pancreas
23	142	Third post-operative day
26	131.5	Sixth post-operative day
27	220	Two years after acute necrosis Post-hæmorrhagic cyst

Sugar Tolerance.—Only once was this test performed, in Case XXVI. The values were 122, 227, 272 and 219 milligrams per 100 cubic centimetres of blood taken at 0, ½, 1 and 2 hours after the ingestion of 1.75 grams of dextrose per kilogram body weight. The tolerance was determined one week after the operation for an acute necrosis of the pancreas and shows a definitely diabetic curve. A total of 4.93 grams of sugar were excreted in the urine. Later determinations are unfortunately not available.

Examination of Peritoneal Exudate or Content of Cysts.—In Case X, which seemed to be a case of chronic fat necrosis with a large and quickly refilling peritoneal exudate and no history of acute attack in the chart, the fluid contained bile, 10 per cent. albumin (due to blood) and cultures were negative. In Case XXII, fluid aspirated from an œdematous pancreas revealed pseudo-diphtheroid bacilli, probably a contamination. Except in those two cases, there is no report of chemical or bacteriological study of the exudate except at autopsy.

In two patients the content of cysts was examined for bacteria and was found sterile in two and four days respectively. No anaërobic cultures were made.

Blood Chemistry.—Aside from the blood-sugar determinations, one re-

FIG. 1.

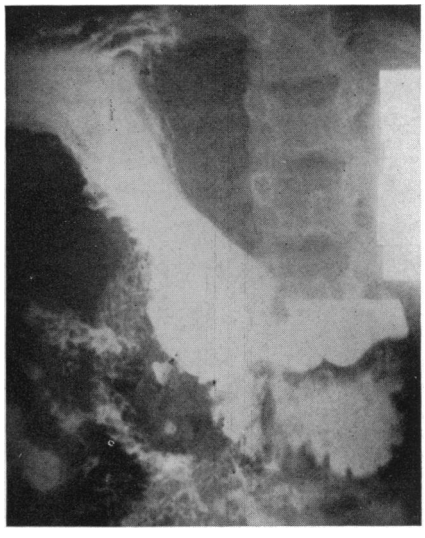

FIG. 2.

FIG. 1.—Case of G. de Takats. Mrs. E. S., aged forty-five. Recurrent attacks of gall-bladder colic with jaundice. Last attack two weeks ago with marked irradiation to the left. Note the irregularity on the greater curvature, which is permanent, and large duodenal curve. At operation a marked enlargement of the head of the pancreas and perigastric adhesions explained the röntgenological findings.

FIG. 2.—Case of G. de Takats. Th. M., aged thirteen. Abscess of the tail of the pancreas, making an impression high up on the greater curvature. The rigid, mottled appearance of the greater curvature simulates malignancy. The abscess was drained toward the flank.

port is available in Case XX of a non-protein nitrogen of 48.4 (normal 35) and a urea nitrogen of 23.3 (normal 15) milligrams per 100 cubic centimetres of blood. This patient had had an operation for pancreatic cyst thirteen years before and returned because of intermittent duodenal obstruction, which was undoubtedly responsible for the high split products. No such determinations are available in acute necrosis of the pancreas, although they would be undoubtedly high.

X-ray examinations are available in five cases. None of these was taken during an acute attack. In acute attacks, the absence of subdiaphragmatic air may exclude gastroduodenal perforation and reveal intestinal obstruction by the aspect of fluid levels. A flat plate on a portable apparatus should

have a definite value in excluding the most frequent conditions that obscure the diagnosis of pancreatic necrosis. Such a diagnosis by exclusion would be very important in determining the optional time of operation, as will be discussed later.

In the absence of acute abdominal symptoms, when a barium meal can be given, the value of X-ray examinations has been emphasized by Case[18] and others. The irregularity on the greater curvature, a pyloric stenosis, a displacement of the transverse colon downwards and stomach upwards, the exaggeration of the duodenal curve are the most frequently observed signs. A few films of our own series serve to illustrate these. (Figs. 1, 2 and 3.)

Time of Operation.—Most statistics bring convincing proof to the effect that in case of acute pancreatic necrosis immediate operation is necessary and that delay raises mortality. Only quite recently have Nordmann, Walzel and Polya expressed their belief that the operation is not capable of arresting the autolytic process and the absorption of protein-split products. They advise against immediate operation and feel that after sequestration or abscess formation, the patient is in far better condition to stand surgical interference. That light cases may be treated conservatively seems uniformly accepted; the discussion centers around the patients, who show from the beginning a severe intoxication and a beginning peritonitis. Previous to their objections, Archibald[19] advocated deferring operation in hyperacute cases with collapse because such patients would not stand the operative interference.

Our cases, although far too limited in number to allow definite conclusions, throw an interesting light on the subject. Table VIII shows the time of operation related to the onset of acute symptoms. It is realized that statistics of this kind are open to criticism; so much depends on other factors, such as the skill of the operator, the severity of the attack, the type of operation, that the time factor alone may not be decisive. However, the immediate operation (less than twenty-four hours) and the late operation (after three weeks) show the lowest mortality. Operations performed in the interval have a mortality of 50 per cent., which is the usually quoted figure in recent mortality statistics (Table I).

TABLE VIII

Time of Operation Related to Onset of Acute Symptoms

Time	Number of Cases	Number of Deaths
Less than twenty-four hours	4	1–25%
Twenty-four to seventy-two hours	2	1–50%
Three days to a week	3	1–33%
One to two weeks	4	2–50%
Two to three weeks	3	2–66%
More than three weeks	5	1–20%

Patients operated on within the first twenty-four hours or after three weeks (nine cases) have an average mortality of 22 per cent.; patients operated on after twenty-four hours but earlier than three weeks (twelve cases) have a mortality of 50 per cent.

That the hyperacute cases may be in shock and have a high red cell count was shown in Table IV. Operation should certainly be deferred in

such patients. In cases that already show evidence of diffuse peritonitis, waiting for localized abscesses would correspond to Ochsner's principles. There is no evidence on hand to show that drainage of the omental bursa, of the biliary tract or of the peritoneal exudate would in any way influence the spreading of necrosis or the virulence of peritonitis. The fulminating cases seem to die, no matter what treatment is instituted; but Nordmann's two cases[20] would indicate that even seemingly moribund patients may be successfully operated on at a later time.

Operation is then most favorable in the early cases that have an œdema of the pancreas without any other involvement; many of these cases subside on conservative treatment and just which would go on to a progressive destruction is impossible to tell. The crux of the situation, however, is this: Can we, with our present diagnostic ability, be sure that we are really dealing with an acute pancreatic necrosis, and not overlooking another type of acute abdominal emergency where delay is fatal? We feel that with a flat X-ray plate gastroduodenal perforation and intestinal obstruction can be excluded; that high blood sugar and high blood diastase content, in the absence of diffuse peritonitis, points to pancreatic involvement with great emphasis. In such patients delay is permissible and may be life-saving; but if in doubt, a rapid exploration is seriously to be considered, if the patient can be brought out of the initial shock.

It is unwise to attempt to lay down hard-and-fast rules for the time of operation, as every case presents a different problem. However, the following principles seem logical to follow.

(1) Never operate on a patient in the initial shock.

(2) If all diagnostic measures point to pancreatic necrosis, delay is permissible, until abscesses localize, cysts or gangrenous parts need removal.

(3) If the diagnosis is uncertain, early operation must be done for fear of overlooking intestinal (appendix) perforation.

(4) If the attack is mild, wait for recovery and then diagnose and operate for biliary-tract infection.

Pre-operative Diagnosis.—Table IX shows the pre-operative diagnosis, as listed on the charts. From this table it is apparent that a diagnosis of acute pancreatic necrosis was not made in one single instance. It is naturally possible that the attending men might have considered such a possibility, but as most hospitals do not require a pre-operative diagnosis from the surgeon before he operates, the interne's diagnosis may be the only one on the chart. Nevertheless, it illustrates the difficulty of diagnosis unless certain laboratory methods will be used. The diagnosis of acute cholecystitis and of common-duct stone has been made in fifteen out of the twenty-two cases, which is essentially correct, being the etiological factor. The involvement of the biliary tract has been found in eighteen out of the twenty-two cases, which gives an 81.2 per cent. incidence of biliary infection as the primary cause. This corresponds to figures given in larger statistics. The diagnosis of intestinal obstruction has been made twice; vomiting and marked colonic distention

are usually present, the transverse mesocolon is œdematous and a paralytic ileus is always present in such sudden retroperitoneal accumulations of fluid. Whether it is ever possible to differentiate this from a mechanic obstruction in the left half of the colon cannot be stated. In such patients, with shock and a low blood-pressure, the use of spinal or splanchnic anæsthesia for diagnostic purposes would not be advisable. Hypertonic sodium chloride solutions overcome paralytic ileus astonishingly well[21] and could be tried. The most important point, however, in ruling out the erroneous diagnoses is the attempt to make a positive diagnosis of acute necrosis of the pancreas by the high fasting blood sugar and high diastase content of the blood. There is only one condition which clinically simulates acute pancreatic necrosis and produces the same laboratory data, and that is a diffuse purulent peritonitis. Unless an appendix-peritonitis or a ruptured ectopic pregnancy can be definitely ruled out, such a possibility must always be kept in mind. The flat X-ray plate will help to diagnose a ruptured viscus by the accumulation of air and the disappearance of liver dullness.

TABLE IX

Pre-operative Diagnosis

In Case of Acute Necrosis		*In Case of Late Sequelæ*		
Acute cholecystitis	12	Pancreatic cyst	2	Correct
Common-duct stone	3	Pyloric obstruction due to previously drained cyst	1	Correct
Intestinal obstruction	2	Carcinoma of pancreas	1	Correct
Post-operative ileus	1	Intestinal obstruction	2	Erroneous
Perforated gastric ulcer	1	Tuberculous peritonitis	1	Erroneous
Ruptured appendix	1	Hepatic cirrhosis with ascites	1	Erroneous
Ruptured ectopic pregnancy	1			
Acute cardiac decompensation	1			
	22		8	

In the late cases, a correct diagnosis has been made in three out of eight instances. These diagnoses were made chiefly possible by the use of a barium meal. In the other cases, the hard nedular pancreatitis, that may follow acute necrosis, gave rise to the diagnosis of carcinoma of the head of the pancreas in one instance. A differentiation of these two conditions may not be possible even on exploration. A biopsy of the inflamed pancreatic tissue is listed as one of the possible causes of acute pancreatic necrosis by Schmieden and Sebening.[4] Peripancreatic adhesions and infiltrated omental tags may produce intestinal obstruction. One of us has seen an abscess in the tail of the pancreas, which produced an obstruction at the splenic flexure. Thus the diagnosis of intestinal obstruction as one of the late sequelæ of acute pancreatic necrosis must be considered and cannot be listed as a diagnostic error. The diagnosis of tuberculous peritonitis and of hepatic cirrhosis with ascites has been made. This is due to the appearance of a large peritoneal exudate in some of the late cases of pancreatic necrosis, where large areas of fat necrosis, thickening of the omentum and infiltration of the mesocolon testify to the origin of this disease. The palpable masses

in the omentum may very easily suggest tuberculous peritonitis, whereas the rapid refilling of peritoneal exudate and perhaps a palpable small liver may suggest portal cirrhosis. That the liver is frequently damaged in acute pancreatic necrosis has already been mentioned and will be discussed later.

Findings at Operation.—Table X indicates the findings at operation, related to mortality. When we compare this table with Table VIII, which deals with the time-factor as related to mortality, we find that early operation (less than twenty-four hours) and early anatomical findings (œdema or hæmorrhagic exudate without necrosis) will give the lowest mortality. Provided the patient is not in shock or can be brought out of it in a few hours, this seems the most logical procedure, although some of these patients would probably recover without an operation. On the other hand, patients with certain pathological findings such as acute liver insufficiency and diffuse peritonitis cannot be benefited by an immediate operation, but probably harmed. Abscess or gangrene, when the patient has overcome the spread of infectious or destructive process, do better when opened late. Post-operative pancreatic necrosis, which occurred after operations on the gastroduodenum or biliary tract, proved fatal in all cases. Here the complication was not recognized, the patient was already weakened by the previous operation and the digestion of ligatures and sutures by pancreatic enzymes played a decisive rôle in the fatal outcome.

TABLE X

Main Pathological Findings at Operations for Acute Pancreatic Necrosis

Findings	Number of Cases	Mortality	
Œdema without necrosis	..	..	
Œdema with fat necrosis	1	..	
Sclerosis with fat necrosis	2	..	
Cyst with fat necrosis	2	..	
Hæmorrhagic exudate	7	1	
	12	1	8.3%
Abscess or gangrene	5	2	
Acute hepatic injury	1	1	
Diffuse peritonitis	1	1	
Post-operative pancreatic necrosis	3	3	
	10	7	70%
Total cases	22	8	36.3%

This table, although the number of cases is small, would again urge operation early, when shock is absent. If, however, the patient is seen at a later stage, expectant waiting is advisable. It is true that some patients will die in this interval, but the number of surgical deaths will be higher. An adequate control-series has not been forthcoming and is very difficult to obtain in clinical cases.

The absence of early œdema without fat necrosis in the operative findings would indicate that the diagnosis has not been made so early or that indica-

tion for surgery was not deemed to be present in this series. In several statistics, [4, 7, 22] patients have been operated on with acute œdema of the pancreas and no other findings with a low mortality. Whether they would have recovered without an operation or gone on to progressive destruction, no one can tell at the onset. Hence again, a very early operation should be postulated.

Surgical Procedures in the Treatment of Pancreatic Necrosis and Its Sequelæ.—The grouping of operations as shown in Table XI may seem arbitrary and the mortality figures not conclusive, as so much depends on the pathological findings. However, the first group with minimal interference shows a comparatively low mortality in spite of the fact that some of the most advanced cases are included in it; whereas the second group, with attempts at drainage of the general peritoneal cavity or extensive surgery on the biliary tract, shows a high mortality. Finally, the third group includes operations for late sequelæ, with no mortality in the three cases.

TABLE XI

Surgical Procedures in the Treatment of Acute Pancreatic Necrosis and Its Sequelæ

Type of Operation	Number of Cases	Mortality	
Exploratory laparotomy, no drainage	2	..	
Cholecystotomy	1	..	
Cholecystectomy	2	..	
Drainage of lesser sack	3	1	
Cholecystotomy plus drainage of lesser sack	*3*	*1*	18%
Cholecystotomy plus drainage of peritoneum	7	5	
Cholecystectomy plus drainage of lesser sack	1	1	
Cholecystectomy plus drainage of common duct	*1*	*1*	77.7%
Gastroenterostomy for pyloric obstruction	1	..	
Drainage of pancreatic cyst	1	..	
Drainage of abscess	1	..	0%

The object of any surgical interference in acute pancreatic necrosis is first of all to drain the infected biliary tract, if that is the primary cause of the disease. Such was the case in over 80 per cent. of this series and is probably even higher if special attention is focused on this source. The drainage of the gall-bladder is the simplest and most rapid form of drainage. While cholecystectomy and common-duct drainage would be the ideal procedure and could be done in patients at an early stage of the disease by skilled surgeons, most patients may not stand so much at the time of acute pancreatic necrosis and should have just as little done as possible. The drainage of the omental bursa and the capsule of the pancreas if it is filled with exudate can do no harm and decompresses the gland. The drainage of the peritoneal cavity is useless and impossible. While arguments are still unsettled as to whether the peritoneal fluid is toxic or protective, it seems to be sterile in the early cases. Later, when permeability changes occur, a diffuse purulent peritonitis is present, containing the flora of the intestinal canal. In either case, drainage is of no avail.

Incision of the capsule or even liberation of the gangrenous portion by the gloved finger has been practiced by many Continental surgeons. Walzel[23] has reported a rupture of the splenic vein following such a procedure, which led to a fatal hæmorrhage and warns of any incisions into the parenchyma itself.

It is interesting to note that a simple exploration, during which the condition was not recognized but where tissue taken for biopsy revealed fat-necrosis, has led to recovery in two instances. This confirms our opinion of spontaneous recovery even in the presence of a large peritoneal exudate.

On the basis of these figures and convincing reports of Nordmann, Heller and others, we would emphasize *biliary drainage* before anything else is done, if infection or stones are recognizable. In case of a large retroperitoneal œdema, this could be drained toward the flank. There is no way of preventing progressive necrosis and intraglandular manipulations may do more harm than good. As secondary operations, removal of the gall-bladder, opening of pancreatic abscesses, removal of sequestrated glands, overcoming pyloric or intestinal obstructions may be done with comparative safety.

Complicating Factors and Their Influence on Mortality.—Table XII lists the complications encountered and diagnosed. Pancreatic asthenia is not listed.[24] The association of parotitis and pancreatitis has been the subject of a great many discussions. We refer to the article of Schmieden and Voss.[25] As following other laparotomies, its appearance is an ominous prognostic sign. The thrombosis of the portal vein or its tributary, the splenic vein, has occurred twice, a portal hypertension with ascites twice. This is not surprising, when one realizes the fulminating destruction of tissue that occurs in the area these veins supply. Surgery is helpless in such a complication. An acute swelling of the liver was seen once during operation. This subject has been thoroughly discussed recently by Henschen,[26] although not in connection with pancreatic disease. It calls for biliary drainage perhaps even through hepatic parenchyma. Our one case recovered.

TABLE XII

Complicating Factors and Their Influence on Mortality of Acute Pancreatic Necrosis

Complications	Number of Cases	Deaths	
Bilateral parotitis	1	1	
Thrombosis of splenic vein	1	1	
Portal thrombosis with infarct	1	1	
Portal cirrhosis with ascites	2	2	
Toxic hepatosis	1	1	
Pleural empyæma	1	..	
Subphrenic abscess	1	..	
Nephrosis with anuria	1	1	
Total complications	9	7	77.7%

Pleural empyæma and subphrenic abscess are not infrequently seen as a late complication. Their adequate drainage resulted in cure. One patient died of an acute kidney-insufficiency with complete anuria. We have referred

to this complication as a sequel to hepatic injury. It is probably part of the general toxæmia.

The Total Mortality Rate.—Of the thirty patients, eleven died, thus giving a mortality of 36.6 per cent. Eight patients were operated on for late sequelæ, which leaves twenty-two cases of acute pancreatic necrosis with eight deaths, a mortality of 36.6 per cent. This is surprisingly less than the statistics shown in the first table, which vary around 50 per cent. It is pos-

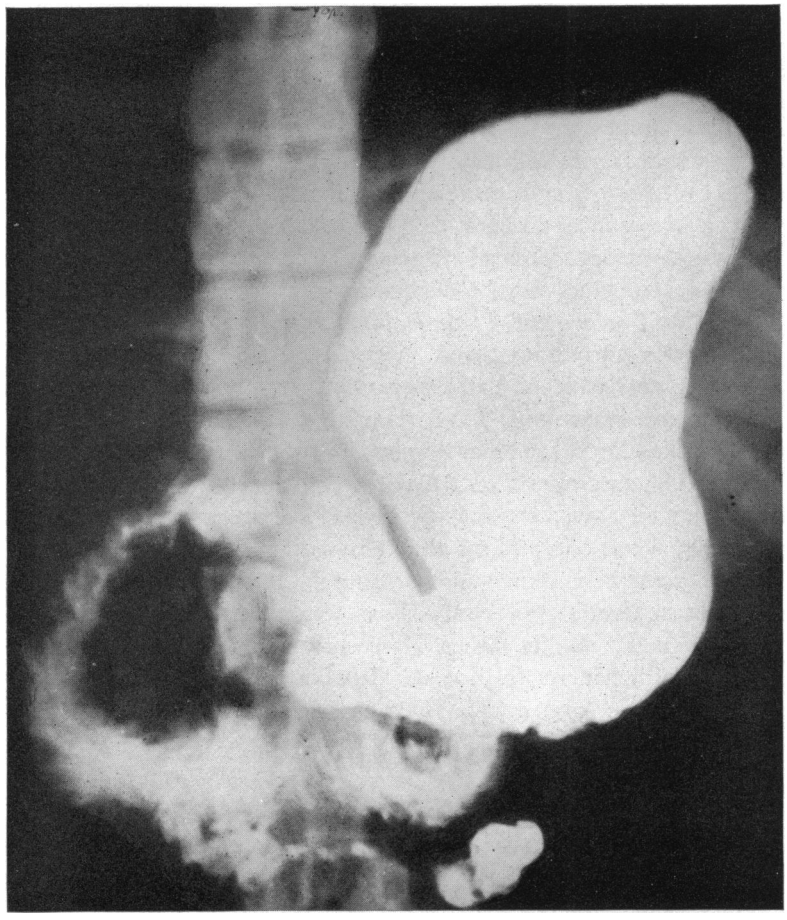

FIG. 3.—Case of G. de Takats. Mrs. E. C. The stomach is large, deformed and empties slowly. The pyloric half of the stomach, on the greater curvature, is displaced upward and toward the left. The duodenal curve is spread out over a larger area than usual. The stomach empties in eight hours. (Report of Dr. J. T. Case.) This was a case of a huge pancreatic cyst, involving the head and body of the pancreas with marked perigastric adhesions. The suture of the cyst wall to the abdominal wall produced a partial pyloric obstruction.

sible that the delay in operating on these non-diagnosed cases unintentionally improved the surgical risk. Also, the frequent use of biliary drainage without any operations on the pancreas, whose involvement has not been suspected at the time of operation, may have improved the statistics. Thus of the twenty-two cases only four came to operation within the first twenty-four hours; whereas in Jung's statistics (*cit.* Guleke[3]) nine out of nineteen, in

Stephan's material four out of eleven and in Zoepffel's cases four out of fourteen came to operation within the first twenty-four hours. Curiously enough, these statistics were compiled to prove that early operation improves the mortality. A glance at Zoepffel's table indicates exactly the same findings that we have arrived at, but interpreted differently: namely, that if the patient is not seen and operated on within the first twenty-four hours, the operation should be deferred to a later period of localizing symptoms. The fact that so many patients die if operated on after twenty-four hours was interpreted as a proof for earlier operation. We are thoroughly in agreement with those who postulate early operation, in the stage of œdema. If, however, necrosis is present, if the patient is first seen three or four days after the acute onset, then conservative treatment, at least for the time being, appeals more to us.

Late Sequelæ of Acute Pancreatic Necrosis.—The patient, who has once gone through an attack of acute pancreatic necrosis, is not safe from late complications. Table XIII lists only one case of recurrent attack, which would be about 4 per cent. of all acute attacks. In reëxamining a number of patients, we frequently hear of recurring epigastric pain, indigestion, nausea and distention. If the biliary-tract infection had been the primary cause, and only an emergency cholecystotomy was done, these recurrent mild attacks indicate a cholecystectomy, and, if necessary, a common-duct drainage. Another cause for recurrent symptoms which requires operation is late sequestration of gangrenous pancreatic tissue, which may have to be removed years after the first operation. The appearance of a persistent pancreatic fistula, with its digestive action on the skin, also needs surgical interference, if it does not close spontaneously in about six months. It may be due to small gangrenous patches of glandular tissue or to a secreting true cyst, whose endothelial lining has not been destroyed. Hohlbaum[27] implanted the secreting pancreatic stump or the wall of the cyst into an upper jejunal loop in three patients. This method deserves serious consideration in suitable cases.

TABLE XIII

Late Sequelæ of Acute Pancreatic Necrosis

	Number of Cases
Recurrent mild attacks	1
Recurrent acute necrosis	1
Persistent fistula	1
Sclerosis of the pancreas	1
Pancreatic cyst	2
Pyloric stenosis following drainage of cyst	2
Diabetes	2
Incisional hernia (6 cases examined)	5

A sclerosis of the pancreas is listed in one case, which had been explored two years after the original attack. There are usually marked digestive disturbances present and a prolonged common-duct drainage or a splitting of the pancreatic capsule, as advocated by Payr and Martina,[28] seem indicated.

No such operations were performed in this series. The operation is not entirely without danger, as acute necrosis and pancreatic fistula may develop after splitting of the adherent capsule.

A pyloric stenosis developed in two cases following suture of the cyst wall to the peritoneum. One patient had a gastroenterostomy, while the other had only a slight intermittent attack of obstruction, although there was a large eight-hour residue of barium. (Fig. 3.) This observation would warn us not to resect too much of the cyst wall in future, as too much tension of the cyst when sutured to the abdominal wall may obstruct the pylorus or cause a marked distortion of the stomach. Two pancreatic cysts have been operated on; both were peripancreatic pseudo-cysts, the results of a previous hæmorrhagic exudate in the omental bursa. A case observed by one of us (de T.) had an acute pancreatic necrosis right after childbirth. The gall-bladder was drained by the obstetrician with the diagnosis of an acute cholecystitis and the pancreas not explored. She was first seen and operated on by us two years later for a large peripancreatic cyst.

Diabetes developed in two cases that have been known to be sugar-free before the acute necrosis set in. This would correspond to almost 10 per cent. of all cases. That latent disturbances of carbohydrate metabolism exist in a larger percentage of cases has recently been frequently discussed.[29]

We were able to obtain post-operative sugar tolerance curves on four other patients, two of which showed abnormally high curves (Chart I). Naturally, the time elapsed since the operation is an important factor, since the great regenerative power of the pancreas, particularly in younger individuals, may overcome even quite serious loss of pancreatic tissue.[30] In older individuals, or in patients who develop a chronic pancreatic sclerosis following acute necrosis with fatty diarrhœa, a decrease in sugar tolerance should be looked for.

One patient had attacks of fatty diarrhœa which could promptly be controlled with tablets of pancreatic extract.

Five out of six patients had an incisional hernia at the site of drainage.

Autopsy Records.—Death occurred in eleven out of thirty cases, a mortality of 36.6 per cent. Of the eleven deaths, seven came to autopsy. The main findings are listed in Table XIV. Pancreatic necrosis was naturally present in all cases as evidenced by gangrenous masses in the gland and fat necrosis spreading through the mesocolon, omentum and not infrequently in perirenal tissue. Its chief spread is through the lymphatics. The peculiar blotchy, lattice-like cyanosis, that is not infrequently present during life, is an important diagnostic sign, according to Walzel,[31] and does not disappear after death. One of us (de T.) has repeatedly seen it on the autopsy table. Its mechanism has never been explained although a stasis of the superficial abdominal veins, accentuated by a sudden increase of pressure in the vena cava, is a possible explanation. There is no fat necrosis in the abdominal wall, but the subcutaneous fat is frequently pale and œdematous.

TABLE XIV

Autopsy Records

Main Pathological Findings in Seven Cases

Findings	Number of Cases	Findings	Number of Cases
Pancreatic necrosis	7	Sero-fibrinous peritonitis	2
Cholelithiasis	4	Purulent peritonitis	2
Common-duct stone	2	Thrombosis of splenic vein	1
Acute cholangitis	1	Portal thrombosis	1
Focal liver necrosis	2	Pleural empyæma	1
Fatty degeneration of the liver	1	General septicæmia	1
Acute yellow atrophy	1	Hæmorrhage into adrenal gland	1

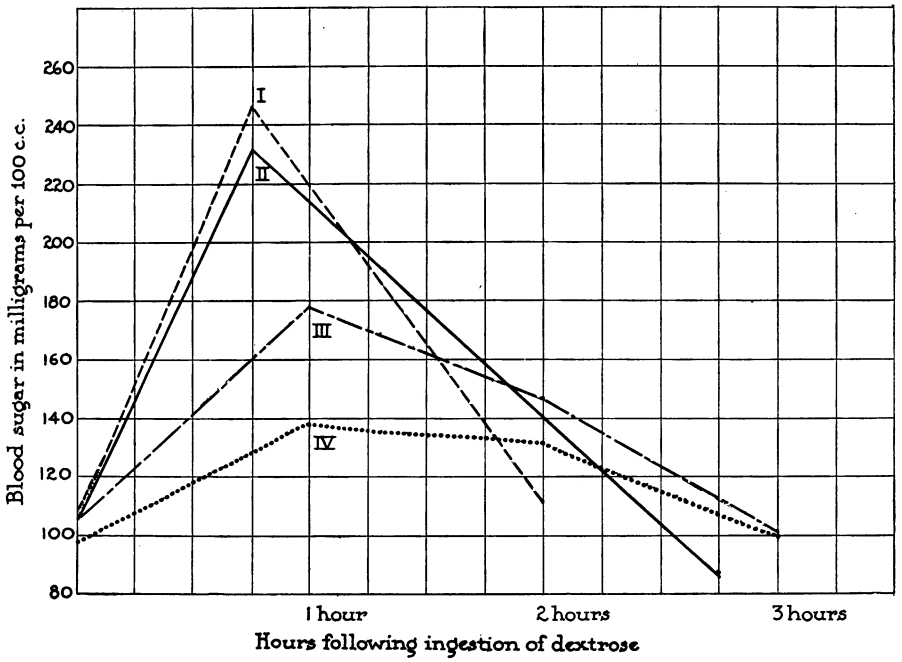

CHART 1.—Sugar-tolerance curves in four patients several years after acute pancreatic necrosis. Cases I and II had fifty grams of dextrose in 25 per cent. solution, and samples of finger-blood were taken at forty-five minutes and two hours. Cases III and IV received 100 grams of dextrose and samples were taken at one, two and three hours. The four curves, then, are not entirely comparable. Nevertheless, it is obvious that the first two patients, in spite of the smaller amount of dextrose, showed a very sharp rise of blood sugar, whereas the latter two show normal peaks. None of these curves can be called diabetic, but the sharp initial rise is suggestive of poor glycogen fixation in the liver and has been seen in mild diabetic cases. (Noorden and Isaac: Die Zuckerkrankheit und ihre Behandlung. Eighth Edition, p. 157, Julius Springer, Berlin, 1927.) The slow fall in Cases III and IV may be due to their age. Case I.—Mrs. J. M., aged forty-eight, six years after operation. Case II.—Mrs. E. G., aged forty-four, seven years after operation. Case III.—Mrs. M. W., aged seventy, seven years after operation. Case IV.—Miss J. J., aged fifty-two, two years after operation.

The high incidence of gall-stones, common-duct stones and biliary-tract infections corresponds to the findings on the operating table. Attention should be drawn to the occurrence of liver damage, which may be the immediate cause of death by hepatic insufficiency.

Peritonitis has been noted in four cases. The exudate is first sterile and later becomes infected by the intestinal flora. The two sero-fibrinous exu-

dates have not been cultured, one of the purulent exudates yielded *B. coli* and anaërobic Gram-positive cocci and bacilli and Gram-negative bacilli. In Brütt's series,[32] the peritoneal exudate was sterile in twelve out of seventeen cases, two showed *B. coli* and three staphylococci. Liver and pancreas were sterile in 64 and 50 per cent. respectively, the rest showed aërobic and anaërobic bacteria. This is of great interest because of Dragsted's[33] work on the importance of anaërobic bacteria in the toxicity of autolytic products. That a sudden gangrene of the pancreas would serve as an excellent medium for previously dormant bacteria is very suggestive, and would explain the rôle of infection in acute pancreatic necrosis. Another source may very easily be the intestinal canal, where permeability changes, probably due to bile-salts, would result in an invasion of bacteria into the peritoneal exudate, as postulated by Andrews.[34] Whether these experimental findings are applicable in man can be settled only by a routine and reliable bacteriological study of exudates found in acute pancreatic necrosis.

Thrombosis of the splenic vein and portal thrombosis have been found once each, but not in the same case. It is surprising that this complication does not occur more frequently, in the presence of such massive, and probably infected tissue destruction. Pleural empyæma was found once. Clinically, one sees not infrequently an immobility of the diaphragm, mostly on the left side, with a serous pleural exudate above it. This accompanies the retroperitoneal and subdiaphragmatic œdema, and through the extensive lymphatic connections through the diaphragm, may easily become infected. Together with subphrenic and perinephritic abscesses pleural empyæma must always be looked for as a complication of acute pancreatic necrosis.

General septicæmia was the cause of death in one case, originating in a diffuse purulent peritonitis. An adrenal hæmorrhage on the left side is noted once. Whether this occurred as an extension of a hæmorrhagic pancreatitis from the tail of the pancreas, or whether it occurred as a terminal phenomenon, cannot be determined from the record. It is, of course, known to occur in virulent infectious diseases with a fatal outcome, and could be clinically suspected by a hypoglycæmia.

Discussion.—*The Pre-operative Diagnosis.*—The difficulty of diagnosis was best illustrated by Table IX, from which it would seem that a positive diagnosis has not been made (at least on the chart) in one single instance. As a routine procedure, not requiring much loss of time or special laboratory facilities, we would recommend the following measures in abdominal emergencies, when pancreatic necrosis is suspected.

(1) *Complete Blood Count.*—High red cell count and hemoglobin mean either dehydration, or, if the attack is hyperacute, gives the degree of shock. High white count rather speaks for acute localized inflammatory reaction; if it is unusually low, and rigidity is present, it is suggestive of peritonitis. High percentage of polymorphonuclear neutrophils signifies the virulence of acute infection. The Schilling-Arneth count will probably not be available

in most hospitals and can certainly not be counted on in emergencies during the night.

(2) *The urine specimen* contains albumen and casts in almost all acute abdominal cases, but the appearance of sugar is suggestive of pancreatic disease. However, it was only present in four out of twenty-two cases, and its absence is certainly not proof against pancreatic necrosis.

(3) *A Blood-sugar Determination.*—A high fasting blood sugar, according to the extensive studies of Krotoske[35] is present in acute pancreatic necrosis. Only a diffuse purulent peritonitis will give such high figures and if that can be eliminated with fair certainty the diagnosis of acute pancreatic necrosis is certain. The figures must be above 160 milligrams to be of any value as smaller elevations might be present with other acute suppurative conditions. We consider a blood-sugar reading, which can be taken by any of the newer micro methods, as the most important aid to a positive diagnosis.

(4) *The Determination of Diastase in Urine and Blood.*—Much has been written recently of the value of diastase determinations in acute pancreatic disease. We refer to only one comprehensive article by Skoog,[36] who made about 3,000 diastase determinations on acute abdominal cases. He determined urinary diastase and felt that while increased values may occur, although seldom, in other acute abdominal conditions, a negative finding, provided the determination is made within twenty-four to thirty-six hours after the onset of symptoms, *excludes any pancreatic pathology.* One of us, with Nathanson,[37] studied the rise in blood diastase following ligation of the tail of the pancreas. The original Wohlgemuth test,[38] modified for clinical purposes, is so simple to run that internes not trained in laboratory work can use it. It is far easier to determine than blood sugar. Because most clinical laboratories are unfamiliar with this test and its value in pancreatic disease, a brief description follows:

Ten cubic centimetres of blood are taken from a vein in a centrifuge tube, allowed to clot and gently centrifuged. Ten test tubes are set up in a rack. One cubic centimetre of serum (or urine) is pipetted into the first and second tubes. One cubic centimetre of 1 per cent. sodium chloride is pipetted into all ten test tubes. After proper mixing of serum and sodium chloride in tube 2, one cubic centimetre is pipetted over into tube 3. Here again, after proper mixing, one cubic centimetre is pipetted into tube 4 and so on up to the tenth tube. The last cubic centimetre pipetted out of the tenth tube is discarded. To every tube two cubic centimetres of a 0.1 per cent. soluble starch solution (Kahlbaum) are added, well mixed, and the whole rack of tubes incubated in a thermostat at 38° C. for thirty minutes. Thus the starch-splitting ferment of the blood can act on the starch solution. At the end of thirty minutes, the fermentation is abruptly stopped by immersion of the tubes in cold water for a few minutes. Three drops of a fiftieth normal iodine solution are added to each tube. The undigested amylodextrin gives a blue reaction, the erythrodextrin red, and the achrodextrin yellow. The end point is read at the tube which shows the first trace of purple without being a solid blue. Suppose this occurs in the fourth

tube. The quantity of diastase in the serum, which was able to digest starch up to that dilution, is calculated as follows: $D=2^4=16_{30}^{38}°$ indicating at the same time the temperature and duration of the incubation. Values between 16 and 32 are normal with this technic. Following experimental duct ligation the diastase has risen to values between 1024 and 3072, which shows the enormous quantities of ferment that can be flooded into the blood-stream when external secretion is obstructed.

We are perfectly aware of the fact that the figures obtained in this manner could be made more accurate. The fact that the serum is incubated

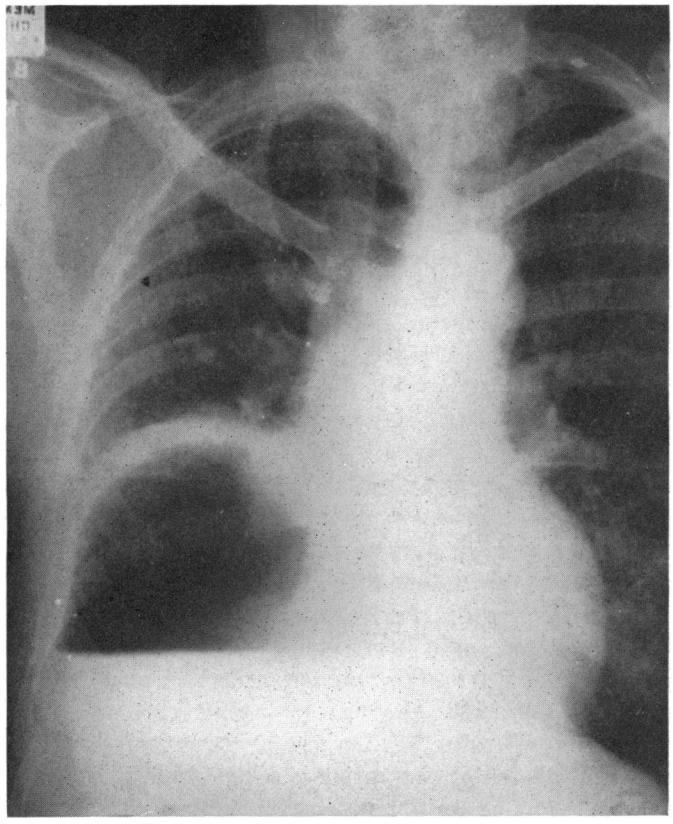

FIG. 4.—Mr. E. C., aged forty-eight. Five days after onset of excruciating pain in upper abdomen, shock, cyanosis, no rigidity. On entrance to the hospital, this large gas bubble was found under the right diaphragm, above a fluid level. The subphrenic abscess was due to a perforation of an ulcer on the lesser curvature. Case of Drs. W. H. Nadler and G. de Takats.

only for thirty minutes and that the starch solution is not buffered to the optimal p_h of diastatic action (7.2) inhibits the action of the ferment. However, the rapidity and simplicity of the test described above makes it possible to use it anywhere, even in the middle of the night, provided the few necessary reagents are ready for use. It is, of course, possible, as Wohlgemuth more recently suggested,[39] to have a starch solution buffered with sodium phosphate to a p_h of 7.2 and to accelerate incubation to fifteen minutes by

using a water bath of 45° C., but we still feel that the test, as described above, serves the purpose of a rapid and adequately reliable orientation.

(5) *Röntgenological Examination.*—In spite of the valuable information that can be gained in obscure abdominal emergencies by films taken by portable X-ray apparatus, such examinations are not carried out often enough. Case,[40] since 1911, has repeatedly emphasized the value of such studies in acute intestinal obstructions, particularly those following operations. An opaque medium is not necessary and the patient is very little disturbed. Laurell[41] has summarized his vast experience with the interpretation of flat films in intestinal obstruction, diffuse peritonitis and localized abscesses. Concerning acute pancreatic necrosis, he believes that a dilatation of the transverse colon and retroperitoneal thickening in the fatty tissue are suggestive, together with a sluggish diaphragm on the left side and exudates in the pleural cavity. A few spoonfuls of barium may bring out the changed contours of duodenal mucosa, and possibly duodenal displacement. Abscesses in the omental bursa can be well visualized.

We have no experience with the positive value of portable X-ray films in a case of acute pancreatic necrosis; however, as a method of excluding mechanical obstruction to the bowel, or gastroduodenal perforation with the characteristic subdiaphragmatic air bubble (Fig. 4) as emphasized by Schnitzler, Vaughan and Singer, its great value is obvious. It may also reveal the characteristic picture of localized peritoneal abscesses long before the clinical symptoms would permit of drainage.

To sum up our aids in pre-operative diagnosis: History of previous gall-bladder attacks, sudden sharp, excruciating pain in the epigastrium with frequent irradiation to the left, often nausea and vomiting, no rigidity, but definite tenderness in the epigastrium with ballooning out of the transverse colon, a marked cyanosis, blotchy and streaky in character. If the patient is in shock, the blood-pressure can hardly be taken. The pulse is empty. The temperature in the early cases is not elevated.

The blood count indicates the degree of dehydration and shock, the urine may contain sugar, but the blood sugar is high and so is the diastase content of the blood. The value of the test for diastase and a portable X-ray film are mainly important for their negative findings, whereby pancreatic necrosis can be excluded.

Pre-operative Management.—If the patient is in shock, as evidenced by the blood-pressure reading and the high red cell count, treatment should be instituted against shock. Small doses of morphine, heat, but chiefly a 6 per cent. gum-acacia solution intravenously will raise the blood-pressure very quickly. In cases of post-operative shock we know of no simpler and more efficient method. The purified gum-acacia solutions are kept in 100 cubic centimetre ampules, diluted to 500 cubic centimetres with normal salt and are free of all previous objections to impurities.[42]

The rapid depletion of liver glycogen, the frequency with which liver damage is found at post-mortem, indicate the administration of dextrose and insulin. This should be given slowly, about 100 grams of dextrose in

10 per cent. solution, together with twenty to thirty units of insulin. Nothing should be administered by mouth, and if there is continuous nausea or repeated vomiting, a Rehfuss tube is passed and the stomach aspirated for retained gastric contents.

As discussed under the indications for operation, an early operation, if the patient is not in shock or has come out of shock, has a low mortality. However, most patients come to the surgeon after more than twenty-four hours have elapsed since the acute onset. If a positive diagnosis of acute necrosis can be made an expectant treatment can be instituted. About 3,000 cubic centimetres of fluid must be given daily; if the patient is obviously dehydrated, 4,000 cubic centimetres. Preferably dextrose-Ringer solution, or dextrose normal salt solution with about one unit of insulin to every three grams dextrose is used. Nothing is given by mouth. If there is considerable intestinal paralysis, twenty cubic centimetres of a 10 per cent. solution of sodium chloride will relieve distention. Under such a régime, even moribund patients may be revived and operations deferred to a later time. If patients die during this time with a peritonitis, an anuria or hepatic insufficiency, no operation could have saved them.

Surgical Procedures.—The anæsthesia is preferably gas-oxygen with local anæsthesia of the abdominal wall. Spinal anæsthesia, particularly in the early cases that may just have been in shock, does not seem advisable. The minimal amount of surgery should consist of draining the biliary tract by cholecystostomy and drainage of the omental bursa. A lumbar drainage through the left flank may be seriously considered, as Lotheisen[43] reports a mortality of 18 per cent. since the routine use of a lumbar drain. The mechanical conditions for drainage are more favorable and a post-operative ventral hernia may be thus avoided.

Post-operative Treatment.—Because of the possible injury to internal secretion, all patients should be watched for a decrease in sugar tolerance and suitable dietary restrictions or even insulin should be administered. The patient should be informed of a possibility of recurring attacks, particularly if the biliary-tract infection has not been radically attended to. In six months to a year following complete closure of the wound, a cholecystectomy, and, if necessary, common-duct drainage should be advised and at the same time the incisional hernia, which almost invariably follows pancreatic drainage, can be attended to. Disturbances of external pancreatic secretion can be ameliorated by potent pancreatic extracts given orally. In patients who develop a late pseudo-cyst or a sclerosis of the pancreas, further surgical procedures must be advised.

Summary.—Thirty cases of acute pancreatic necrosis or their sequelæ have been discussed. The uncertainty of pre-operative diagnosis and the high mortality challenge to further efforts in this field. A routine use of blood-sugar and blood-diastase determinations together with a frequent employment of flat X-ray plates may greatly improve our diagnostic ability. The proper time of operation and the selection of the proper surgical methods will diminish mortality. Attention should be focused to late sequelæ of acute

pancreatic necrosis, some of which can be prevented. A prophylaxis of acute pancreatic necrosis for the large majority of cases lies in early surgical treatment of biliary-tract infection.

We wish to express our deep gratitude to the staffs of Evanston and Wesley Memorial Hospitals and particularly to Drs. Charles A. Elliott, William R. Parkes and Harry M. Richter for the privilege of obtaining follow-up records of their patients.

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